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PATENT SPECIFICATION

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COMPLETE SPECIFICATION

NO DRAWINGS

Pharmaceutical Formulations for Oral Administration to Animals

We, PFIZER LIMITED, a British Company, of Ramsgate Road, Sandwich, Kent (formerly of 137-139 Sandgate Road, Folkestone, Kent), do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement :—

The present invention relates to formulations containing physiologically active substances and in particular to formulations suitable for oral administration to animals.

It is difficult to administer solid physiologically active substances to animals as they often spit out a pill or tablet very shortly after administration, unless the pill or tablet is shot down the animal's throat or unless the animal's muzzle is held closed until the pill or tablet is swallowed ; this is often difficult to achieve, particularly with larger animals. It may also be necessary to raise the animal's head to cause the pill or tablet to pass down the gullet more easily, and this may also be difficult with large animals such as cattle.

It is an object of the present invention to provide an improved formulation for oral administration.

According to the present invention there is provided a solid formulation suitable for oral administration to animals, being in the form of wafers readily adherent to the tongue or buccal mucosa and comprising a physiologically active substance, a solid non-toxic adhesive, and a non-toxic humectant and plasticiser.

The physiologically active substance may be relatively water-insoluble, for example, finely divided metallic iron and/or other metal, such as copper, or compounds thereof, a corticosteroid, a phenothiazine, or a water-insoluble sulphonamide or vitamin. The active substance may be a water-soluble substance, for example, an antibiotic such as a penicillin salt or a tetracycline antibiotic, a hormone or a water-soluble vitamin or sulphonamide. Relatively water-insoluble compounds are absorbed when the formulation breaks up in the mouth and passes through the alimentary system. Water-soluble compounds are absorbed also through the mucous membranes of the mouth.

Among solid non-toxic adhesives which may be used are, for example, sodium carboxymethylcellulose and other cellulose derivatives such as hydroxyethylcellulose ; water-soluble polyoxyethylene resins ; non-toxic vegetable gums, for example, gum tragacanth, gum acacia and gum karaya ; and metallic silicates such as sodium silicate and hydrated aluminium silicate ; isinglass ; agar-agar ; water-soluble alginates ; gelatine ; casein ; albumen and other proteins.

The humectant and plasticiser is preferably a polyol such as sorbitol, glycerol, propylene glycol or dipropylene glycol ; polyoxyalkylated polyols, for example polyoxyethylated sorbitols, polyoxyethylated glycols and polyoxyethylated glycerol ; a-methylglycerol ; corn syrup ; or propylene glycol glucoside. The humectant and plasticiser may be incorporated into the adhesive or into the solid physiologically active substance before mixing with the other ingredient or ingredients, or all ingredients may be mixed together before forming into the desired wafers.

The formulation may also contain in addition to the above, other non-toxic ingredients, for example water, to obtain the correct consistency before forming.

The presence of the adhesive ensures that the formulations of the present invention

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adhere to the tongue or to the inside of the cheek or palate, thus rendering them difficult to spit out when placed into the mouth of the animal. The presence of the humectant and plasticiser gives flexibility to the wafers so that they can conform more closely to the surface of the tongue or buccal mucosa. It also ensures that saliva is rapidly absorbed to increase the adherence of the wafer.

By forming the formulation into wafers of relatively large surface area, for example greater than 300 square millimetres and of a thickness from 0.2 millimetres to 1.0 millimetre, a product is obtained which gives excellent adhesion to the tongue or buccal mucosa and which is thus particularly difficult to spit out.

The relative proportions of the physiologically active substance, the adhesive and the humectant and plasticiser in the formulation may vary widely, depending upon the substance used. For example, the proportion of the humectant and plasticiser may be conveniently from 5% to 40% by weight based on the total weight of the formulation and the proportion of the adhesive may conveniently be from 1% to 10% by weight based on the total weight of the formulation.

The following Examples further illustrate the present invention.

Example 1

60 parts by weight of reduced finely divided iron, 0.6 part by weight of copper powder, 6 parts by weight of low viscosity sodium carboxymethylcellulose, 20 parts by weight of sorbitol solution (70% solids) and 92 parts by weight of water were mixed, and the mixture was rolled to form a sheet of paste. This was heated to remove excess moisture and then sub-divided into 200 separate portions. Each portion was a wafer, 21 millimetres in diameter and 0.38 millimetre thick.

These wafers were tested upon young piglets as follows. Litters were divided into two equal groups which were reared in the same manner, except that each piglet of one group had a wafer placed in its mouth at the age of five days and again at the age of 12 days; the piglets of the other group were not so treated.

The piglets were unable to spit out the wafers, even though no effort was made by the person administering them to prevent this, and each wafer gradually disintegrated in the mouth and passed down the throat. Blood tests carried out after a similar period on the treated and untreated piglets showed a considerably higher haemoglobin level and red blood cell count in the treated piglets than in the untreated piglets, thus demonstrating that the iron had been successfully assimilated.

Example 2

6.25 parts by weight of calcium dioxytetracycline, 6 parts by weight of low viscosity sodium carboxymethylcellulose, 5 parts by weight of sorbitol "C" syrup, 0.4 part by weight of "Tween 80" and 19.9 parts by weight of water were mixed and the mixture was subdivided into 50 wafers of a size similar to those described in Example 1. "Tween 80" is a polyoxyethylated sorbitol compound and the word "Tween" is a Registered Trade Mark.

The wafer adhered to the inside of the mouth and was very difficult to spit out when it had been orally administered.

It will be understood that, although reference has been made herein to the humectant and plasticiser as a single substance i.e. to a substance which fulfils both functions, it is possible to use two substances one of which is a humectant and the other of which is a plasticiser and that therefore the term "humectant and plasticiser" when used in a general sense is intended to cover either a single substance or two substances as above referred to.

WHAT WE CLAIM IS:—

1. A solid formulation suitable for oral administration to animals, being in the form of wafers readily adherent to the tongue or buccal mucosa and comprising a physiologically active substance, a solid non-toxic adhesive, and a non-toxic humectant and plasticiser.

2. A formulation as claimed in Claim 1 wherein the solid non-toxic adhesive is sodium carboxymethylcellulose, hydroxyethylcellulose or other cellulose derivative; a water-soluble polyoxyethylene resin; gum tragacanth, gum acacia, gum Karaya or other non-toxic vegetable gum; sodium silicate, hydrated aluminium silicate or other non-toxic metallic silicate; isinglass; agar-agar; a water-soluble alginate; or gelatine, casein, albumen or other proteins.

3. A formulation as claimed in either of the preceding Claims wherein the humectant and plasticiser is sorbitol, glycerol, propylene glycol, dipropylene glycol or another polyol, a polyoxyethylated sorbitol, polyoxyethylated glycol, polyoxyethylated glycerol, or other polyoxyalkylated polyol; a-methylglycerol; corn syrup or propylene glycol glucoside.

4. A formulation as claimed in any of the preceding Claims in the form of wafers having surface area greater than 300 square millimetres and a thickness from 0.2 millimetre to 1.0 millimetre.

5. A formulation as claimed in any of the preceding Claims wherein the proportion of the humectant and plasticiser is from 5% to 40% by weight based on the total weight of the formulation.

6. A formulation as claimed in any of

the preceding Claims wherein the proportion of the solid non-toxic adhesive is from 1% to 10% by weight based on the total weight of the formulation.

7. A formulation according to any of the preceding Claims in which the physiologically active substance is iron or a compound thereof.

8. A formulation according to Claim 7 which contains copper or a compound thereof in addition to the iron or compound thereof.

9. The solid wafer formulation suitable for oral administration to animals substantially as described in Example 1.

10. The solid wafer formulation suitable for oral administration to animals substantially as described in Example 2.

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